REMARKS

With this amendment, claims 1-38 are pending.

Claims 18 and 19 have been amended to correct typographical errors. Support for the amendment to claim 18 may be found, for example, in the specification as filed at page 10, paragraph [0042]. Support for the amendment to claim 19 may be found, for example, in the specification as filed at pages 19-20, paragraph [0058].

I. Claim Objections

Claims 18 and 19 are objected to by the Office and correction of the same is requested. For purposes of Examination, the Office notes that it interpreted claim 18 to recite the phrase "a buffered dye solution" and claim 19 to recite the phrase "a quencher."

The above-recited interpretations used by the Office for purposes of examination are correct. Consistent therewith, Applicants have amended claims 18 and 19 with this amendment. Specifically, claim 18 has been amended to replace the term "bye" with the term "dye" such that the claim now recites the phrase "a buffered dye solution," and claim 19 has been amended to delete the term "the" such that the claim now recites "a quencher." Accordingly, the Office's objection as applied to claims 18 and 19 is rendered moot.

II. 35 U.S.C. 103(a)

Claim 1 is directed to a process for staining sperm cells. The process comprises forming a staining mixture containing intact viable sperm cells and a DNA selective fluorescent dye and subjecting the staining mixture to a temperature in excess of 40°C.

Neither Seidel et al. or Johnson discloses a process for staining sperm cells wherein a staining mixture containing intact viable sperm cells and a DNA selective fluorescent dye is subjected to a temperature ***in excess of 40 °C***. In the absence of disclosing each and every element of the claimed invention, a *prima facie* case of obviousness cannot be established.

Notably, the claimed process allows for the staining of ***viable*** sperm cells in less time than is required to stain cells at lower temperatures. This advantage rests upon Applicants' surprising discovery that sperm cells can be stained with a dye for use in flow cytometry processes at temperatures in excess of 40°C in less time than is required to stain the cells at lesser temperatures ***without significant impact upon sperm cell viability***.[1] This is demonstrated, for example, in Figures 3D and 7B, described in Examples 3[2] and 7,[3] respectively, wherein it is illustrated that the fluorescence intensity of sperm cells stained in 60μM Hoechst 33342 at 43°C plateaus after about 25 to 30 minutes of staining (Figure 3D) without significant impact on the motility and progressive motility of the cells (Figure 7B). Likewise, Figures 4A and 9B, described in Examples 4[4] and 9,[5] respectively, illustrate that the fluorescence intensity of sperm cells stained in 80μM Hoechst 33342 at 43°C plateaus after about 15 minutes of staining (Figure 4A) without significant impact on the motility and progressive motility of the cells (Figure 9B). Figures 5A and 9C, described in Examples 5[6] and 9,[7] respectively, illustrate the same phenomena for sperm cells stained in 80μM Hoechst 33342 at 43°C, with fluorescence intensity reaching a plateau after about 10 minutes of staining (Figure 5A) without significant impact on the motility and progressive motility of the cells (Figure 9C). Figures 5B and 10C, described in Examples 5[8] and 10,[9] respectively, also illustrate the same phenomena for sperm cells stained in 100μM Hoechst 33342 at 45°C, with fluorescence intensity reaching a plateau after about 5 minutes of staining (Figure 5B) without significant impact on the motility and progressive motility of the cells (Figure 10C). It is against this backdrop, and in light of scope and content of the prior art, the differences between the prior art and the claimed methods,

[1] Specification as filed, page 7, paragraph [0036].
[2] Specification as filed, beginning at page 26, paragraph [0068].
[3] Specification as filed, beginning at page 29, paragraph [0076].
[4] Specification as filed, beginning at page 27, paragraph [0070].
[5] Specification as filed, beginning at page 30, paragraph [0078].
[6] Specification as filed, beginning at page 28, paragraph [0072].
[7] Specification as filed, beginning at page 30, paragraph [0078].
[8] Specification as filed, beginning at page 28, paragraph [0072].
[9] Specification as filed, beginning at page 30, paragraph [0079].

and the level of ordinary skill in the art,[10] that the nonobviousness of the present invention must be reviewed.

The Office cites two primary references as the basis of each of its six obviousness rejections. Seidel et al. disclose methods of staining sperm cells, and in particular frozen-thawed sperm cells, "to allow increased resolution of X-chromosome bearing from Y-chromosome bearing spermatozoa resulting in high purity X-chromosome bearing and high purity Y-chromosome bearing populations of sperm cells" upon separation of the same.[11] Generally, separation occurs via flow cytometry. In a particular embodiment, Seidel et al. disclose staining of spermatozoa with Hoechst 33342 dye at a concentration of greater than about 40μM at a temperature between about 30°C and about 40°C for about 200 minutes,[12] with Hoechst 33324 dye at a concentration between 40μM and 2500μM at a temperature between about 30°C and about 40°C for between 50 and 200 minutes,[13] and with Hoechst 33324 dye at a concentration between about 200μM and 2500μM at a temperature of about 37°C for between about 60 and about 190 minutes.[14] Seidel et al. further disclose a particular embodiment wherein frozen-thawed bovine spermatozoa are stained in Hoechst 33342 at a concentration of 2240μM and incubated for about 60 minutes at a temperature of about 39°C.[15] While Seidel et al. disclose working examples wherein samples of frozen-thawed bull sperm from two different bulls were stained in 224μM and 2240μM of Hoechst 33342 for 190 minutes and 60 minutes, respectively, ***there is no indication of the temperature at which these frozen-thawed sperm samples were stained***.

Johnson discloses the separation of intact X and Y chromosome-bearing sperm populations according to DNA content using a flow cytometer/cell sorter into X and Y chromosome-bearing sperm enriched populations. The sperm cells are combined with a DNA selective dye at a temperature of 30°C to 39°C.[16] Johnson discloses incubation

[10] Graham v. John Deere Co., 86 S.Ct. 684, 694 (1966).
[11] Seidel et al. (U.S. Patent Application Publication US 2004/0049801) at paragraph [0032].
[12] Seidel et al. (U.S. Patent Application Publication US 2004/0049801) at paragraph [0035].
[13] Seidel et al. (U.S. Patent Application Publication US 2004/0049801) at paragraphs [0036] and [0048].
[14] Seidel et al. (U.S. Patent Application Publication US 2004/0049801) at paragraph [0037].
[15] Seidel et al. (U.S. Patent Application Publication US 2004/0049801) at paragraph [0037].
[16] Johnson (U.S. Patent No. 5,135,759), column 4, line 41, and claims 1, 19, and 20.

for a period of 1 hour at 35°C,[17] 1 hour at 39°C,[18] and 1.5 hours at 30°C.[19] In Example 1, Johnson reports a staining and sorting procedure wherein the sperm cells were incubated in Hoechst 33342 at a concentration of 5μM for 1 hour at 35°C.[20]

As noted above, each and every element of the claimed invention is not disclosed in Seidel et al. or Johnson, either individually or in combination, as neither discloses the staining of viable sperm at a temperature in excess of 40°C. Realizing that each and every element of the claimed invention is not present in these references, the Office relies upon an argument of optimization to supports its 103(a) rejection. Specifically, the Office asserts that Applicants have merely optimized the temperature at which the claimed process is to be performed. A review of the art of record, however, bears out the fact that the claimed invention is anything but the result of optimization.

The cited art merely discloses that cells may be stained at a range of temperatures from about 30°C to about 40°C. One may presume this to be possible, as sperm cells typically exist physiologically in the testes at a temperature of, for example, about 31°C to about 35°C in human males,[21] and, for example, in the human vagina upon insemination at temperatures of about 37°C to 38°C (typical human body temperature). While one skilled in the art may, therefore, reasonably conclude that sperm cells may be subjected to staining temperatures in the range of about 31°C to about 38°C (the typical range of temperatures to which sperm are physiologically subjected), and perhaps even as high as 39°C as disclosed and claimed in Johnson, without significant impact on sperm cell viability, one skilled in the art would have no reason to conclude that sperm cells could be subjected to staining temperatures in excess of 40°C without significant impact on sperm cell viability. This is demonstrated by the fact that none of the art of record discloses the staining of sperm cells at a temperature in excess of 40°C, even though approximately 70% of the art of record was published ***after*** the publication of Johnson.

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[17] Johnson (U.S. Patent No. 5,135,759), column 4, line 40, and claims 7 and 25.
[18] Johnson (U.S. Patent No. 5,135,759), column 4, line 43, and claims 6 and 24.
[19] Johnson (U.S. Patent No. 5,135,759), column 4, line 43, and claims 8 and 26.
[20] Johnson (U.S. Patent No. 5,135,759), column 6, lines 32-33.
[21] *See*, for example, Partsch, C-J. et al., Arch Dis Child, 83: 364-368 (2000), wherein it is stated that "[t]he physiological temperature of the adult human testis has been reported as being between 31 and 35°C" (copy enclosed).

Particularly telling, and further confirming this point, is the prosecution history of Johnson,[22] one of the primary 103(a) references cited by the Office. The Johnson application was originally filed with a single independent claim directed to a method of preselecting the sex of mammalian offspring. This claim contained the step of "b) staining said sperm with a fluorescent dye capable of selectively staining DNA in living cells."[23] In response to an Office action stating that the claimed invention was obvious,[24] Johnson cancelled claim 1 as filed and added independent claim 7. New claim 7 contained a staining step that required

> a) staining sperm collected from a male mammal with a fluorescent dye capable of selectively staining DNA in living cells **by incubating the sperm with the dye at a temperature in the range of about 30°-39°C**;[25]

At the time of this amendment, Johnson stated that

> [t]he claims as now amended require that the dye staining be conducted in the temperature range of about 30°-39°C. As previously mentioned, this temperature range is ***critical*** for the purpose of obtaining effective staining to achieve discrimination between male sperm and female sperm ***while preserving viability***."[26]

Thereafter, the Office issued a final Office action rejecting, *inter alia*, claim 7 as being obvious in light of cited art, the Office asserting that

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[22] A copy of this prosecution history is submitted herewith. It is also being made of record by the filing of a Supplemental IDS concurrently herewith.
[23] Johnson (U.S. Patent 5,135,759) file history, application as filed, claim 1.
[24] Office Action of March 28, 1990. The dates of all Office actions referred to herein are determined based upon the mailing date of the same.
[25] Amendment of July 26, 1990, at page 1, emphasis added. The dates of all amendments referred to herein are determined based upon a date stamp indicating the date the amendment was received at the USPTO.
[26] Amendment of July 26, 1990, at pages 4-5 (emphasis added).

> [t]he reference states that the sperm was incubated at room temperature. In the absence of a showing of unexpected result, the incubation of sperm at temperatures of 30-39°C is well within the skill of the practitioner such that, as sperm exists physiologically in the testis at temperatures around 35°C and in the vagina at temperatures around 37-38°C, it would have been obvious to one of ordinary skill in the art to incubate sperm at temperatures at which sperm exists physiologically.[27]

Johnson thereafter filed a continuation application and preliminary amendment in which all previous claims were canceled and new claims 9-27 were presented. The two independent claims, 9 and 27, each contained a staining step that further limited the staining as compared to cancelled claim 7. Specifically, each of these two claims now required

> a) staining sperm collected from a male mammal with a fluorescent dye capable of selectively staining DNA in living cells **by incubating the sperm with the dye at a temperature in the range of about 30°-39° C** for a period of time sufficiently long for staining to take place uniformly but sufficiently short **to preserve viability of the sperm**;[28]

Again, Johnson stressed the criticality of staining the cells at the recited temperature, noting that

> [t]he present claims require that dye staining be conducted in the temperature range of about 30°-39°C. See, e.g., claims 9, 14-16, and 27. This temperature range is ***critical*** for the purpose of obtaining effective staining to achieve discrimination between Y-bearing sperm and X-bearing sperm while ***preserving sperm viability***.[29]

[27] Office Action of November 20, 1990, at pages 2-3.
[28] Amendment of April 26, 1991, at page 1 (emphasis added).
[29] Amendment of April 26, 1991, at page 7 (emphasis added).

About one month later and before the Office examined the newly presented claims, Johnson filed a "preliminary response." The preliminary response consisted of remarks prepared by Johnson's attorney and a declaration by the applicant, Johnson. This declaration was submitted "for the purpose of establishing the ***criticality*** of incubating sperm at temperatures ranging from 30°-39° C prior to sorting as required by the claims of record."[30]

In response to the preliminary amendment and preliminary response, the Office again rejected all pending claims, based in part on the *Handbook of Histopathological and Histochemical Techniques*,[31] noting that this particular reference disclosed the fact that "[a] reduction in staining time of certain procedures may usually be effected by the application of heat."[32] According to the Examiner:

> Even though this reference is drawn particularly to histological staining techniques, it appears that the incubation of sperm at temperatures of 30-39°C in order to reduce staining time is, in the absence of objective evidence to the contrary, well within the skill of the practitioner such that it would be expected that an increase in the temperature during the staining of sperm would result in a decreased staining time. As sperm exists physiologically in the testes at temperatures around 35°C and in the vagina at temperatures around 37-38°C and in expectation of the fact that sperm are very short-lived cells, it would have been obvious to incubate sperm at temperatures at which sperm exists physiologically in order to minimize holding time prior to separation and insemination.[33]

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[30] Preliminary Response of May 30, 1990, at page 1 (emphasis added).
[31] Cullling, Handbook of Histopathological and Histochemical Techniques, 3rd Ed., Butterworths & Co. (1974), page 192 (copy enclosed).
[32] Office Action of September 6, 1991, at page 2.
[33] Office Action of September 6, 1991, at page 2.

In response to this rejection, Johnson amended the independent claims that contained a staining step (independent claims 9, 27, and 28[34]), adding the phrase "intact, viable" to describe the mammalian sperm to be stained and sorted. Furthermore, with respect to the citation to the *Handbook of Histopathological and Histochemical Techniques*, Johnson asserted there is no suggestion therein that the described techniques could be applied to sperm cells.[35] According to Johnson,

> The technique discussed in the handbook relates to cells being prepared for mounting. These cells are ***typically nonliving and are often in some way disrupted***. Moreover, there is ***no attempt to preserve viability*** of cells being mounted for histopathological or histochemical purposes. ***Except at the very low end of the 37-57° C range indicated in the reference, sperm cells would immediately be killed.*** As discussed above, applicants have successfully stained living cells **without substantially affecting their viability**. This is considered to be objective evidence in support of an unexpected result.[36]

That Johnson, presumably one of ordinary skill in the art, limited the staining temperature of the sperm cells to 30°C to 39°C while ***repeatedly arguing the criticality of the staining temperature to maintaining the viability of the stained cells*** further demonstrates that Applicants have not merely optimized the staining temperature of a known process and, furthermore, that their presently claimed invention is nonobvious in light of the cited art. In fact, a review of the prosecution history of Johnson, a document that became publicly available as of the August 4, 1992, issue date of Johnson, would teach away from the claimed invention, as it discloses that staining in excess of the disclosed 39°C staining temperature is detrimental to the preservation of sperm viability.

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[34] Independent claim 28, as well as dependent claims 21-34, were added via Preliminary Amendment dated June 25, 1991, in response to a telephone interview with the Examiner on May 30, 1991.
[35] Amendment of January 16, 1992, at page10.
[36] Amendment of January 16, 1992, at page 10 (emphasis added).

A prima facie case of obviousness, even when based upon a theory of optimization, cannot be maintained when the art teaches away from the claimed invention.[37]

In the absence of being able to demonstrate the obviousness of Applicants' claimed invention based on the cited art, the Office has instead utilized Applicants' specification as a template for achieving the claimed invention in. This form of "hindsight," however, is neither permissible nor the standard for determining obviousness.[38]

Accordingly, staining sperm cells at temperatures in excess of 40°C as presently claimed cannot be said to be a mere optimization of the staining temperatures disclosed in the cited art, as the art of record would indicate to one skilled in the art that (1) the temperature range at which the claimed process is performed is ***outside of the then known range*** of temperatures for staining sperm cells and (2) the staining of sperm cells at temperatures ***in excess of the then known range*** of temperatures would be ***detrimental to the sperm cells***.

A. Claims 1-23 and 29-38 over Seidel et al. or Johnson in view of D'Occhio, Guthrie et al., Garner et al., Sabeur et al., De Pauw et al., Bruemmer et al., or Remington

Reconsideration is requested of the rejection of claims 1-23 and 29-38 under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. or Johnson in view of D'Occhio[39] with respect to claims 1-17, 19, and 20; in view of Guthrie et al.[40] with respect to claims 1-17 and 19-22; in view of Garner et al.[41] with respect to claims 1-20 and 23; in view of Sabeur et al.[42] or De Pauw et al.[43] in further view of Bruemmer et al.[44]

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[37] *See*, *In re Geishler*, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997) (a *prima facie* case of obviousness based on a theory of optimization may be rebutted if Applicant "(1) can establish 'the existence of unexpected properties in the range claimed' or (2) can show 'that the art in any material respect taught away' from the claimed invention." (citing *In re Malagari*, 182 USPQ 549, 553 (CCPA 1974))).
[38] *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1532 (Fed. Cir. 1988); *In re Yates*, 663 F.2d 1054, 1057, 211 U.S.P.Q. 1149, 1151 (C.C.P.A. 1981).
[39] D'Occhio, Animal Breeding: Use of New Technologies, Chapter 19: 247-264 (1999).
[40] Guthrie et al., Molecular Reproduction and Development, 61(1): 87-92 (2002).
[41] Garner et al., Biology of Reproduction, 53: 276-284 (1995).
[42] Sabeur et al., Journal of Reproduction and Fertility, 120: 135-142 (2000).
[43] De Pauw et al., Biology of reproduction, 67: 1073-1079 (2002).
[44] Bruemmer et al., Journal of Animal Science, 80(1): 12-18 (2002).

with respect to claims 1-15 and 29-34; and in view of Remington et al.[45] with respect to claims 1, 29, 30, 31, and 35-38.

Against the backdrop discussed above with respect to Seidel et al. and Johnson, it cannot be maintained that the claimed invention is obvious in light of the secondary references the Office combined therewith. Specifically, D'Occhio discloses that sperm are typically diluted in a species specific semen buffer[46] and incubated with 7.0mM to 9.0mM Hoechst 33342 at 32°C to 35°C for 45 to 60 minutes,[47] noting that propidium iodide is often included in the mixture during incubation to quench the fluorescence of the Hoechst 33342 in the dead sperm. Guthrie et al. disclose the comparison of staining and sorting of boar sperm cells at two different laser power outputs (25mW and 125mW) wherein prior to sorting, the cells are incubated in 28μM (final concentration) of Hoechst 33342 at 35°C for one hour and treated with 50μM (final concentration) of FD&C#40 food coloring to quench the Hoechst 33342 fluorescence of the dead sperm. Garner et al. disclose the staining of sperm from bulls, boars, rams, rabbits, mice, and men in a composition of SYBR-14 and propidium iodide and the use of flow cytometry to quantify the proportions of living and dead sperm. Sabuer et al. and De Pauw et al. disclose the use of TALP as a sperm buffer and the staining of sperm with Hoechst 33342 (Sabeur et al.) or SYBR-14 (De Pauw et al.). Bruemmer et al. disclose the use of pyruvate in a stallion sperm diluent. And Remington et al. disclose the use of vitamin K_3 and the lipoamined-lipoamide dehydrogenase couple as redox agents. ***Notably, none of these secondary references discloses the staining of viable sperm cells at a temperature in excess of 40°C***. Accordingly, the failure of Seidel et al. and Johnson to render the claimed invention obvious is not remedied by any of these secondary references, either alone or in combination, as each and every element of the claimed invention is not present in the art. As such, a *prima facie* case of obviousness has not been demonstrated.

[45] Remington et al., International Application Publication No. WO 02/077011 (also published as U.S. Patent No. 7,015,310).
[46] Citation to Johnson, Reprod Fertil Dev., 7: 893-903 (1995) for this proposition.
[47] Citation to Johnson et al., Gamete Res., 17: 203-212 (1987) for this proposition.

Claims 2-23 and 29- 34, which depend from claim 1, are patentable over Seidel et al. or Johnson in view of D'Occhio, Guthrie et al., Garner et al., Sabeur et al., De Pauw et al., Bruemmer et al., or Remington et al. for the reasons stated with respect to claim 1 and by reason of the additional requirements each claim introduces.

B. Claims 1-15, 24, and 28 over Seidel et al. or Johnson in view of Van Demark et al. or Salisbury et al.

Reconsideration is requested of the rejection of claims 1-15, 24, and 28 under 35 U.S.C. 103(a) as being unpatentable over Seidel et al. or Johnson in view of Van Demark et al. (U.S. Patent No. 3,005,756) or Salisbury et al. (Journal Reproductive Fertility, 6: 351-359 (1963)).

Van Demark et al. discloses a diluent containing sodium citrate dihydrate, sodium bicarbonate, potassium chloride, glucose, sulfanilamide, penicillin dihydrostreptomycin sulfate, and sufficient egg yolk to make a final diluent consisting of 10% to 15% egg yolk and saturated with CO_2 (termed "IVT diluter"). Van Demark et al. disclose that sperm stored in the IVT diluter demonstrate an increased motility over a one to seven day period of time versus sperm stored in a control diluent. Van Demark et al. also disclose that the fertility of the sperm stored in the IVT diluter did not decrease during a six to seven day storage period at room temperature whereas the sperm stored in a control diluter at low temperatures decreased after one to two days in storage and was ineffective after four days of storage.

Salisbury et al. disclose the use of several different compositions comprising sodium bicarbonate ($NaHCO_3$), potassium bicarbonate ($KHCO_3$) and citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$) in order to perform certain metabolic studies to determine the role of "various substrates in the metabolism and economy of the spermatozoon."[48] Salisbury et al. disclose the collection of bull ejaculates into a collection diluent A consisting of 1.4926g $NaHCO_3$, 0.9231g $KHCO_3$, and 1.890g $C_6H_8O_7 \cdot H_2O$ in water (100ml), a collection diluent B consisting of 0.8146g $NaHCO_3$, 1.7301g $KHCO_3$, and 1.890g $C_6H_8O_7 \cdot H_2O$ in water (100ml), and a collection diluent C consisting of 0.9%

[48] Salisbury et al., page 352, first full paragraph.

NaCl. The air phase above diluents A and B was replaced by gassing with 100% carbon dioxide, while the phase above diluent C was air (control). Metabolic studies were performed on the cells from each of the diluents after the cells were removed from their respective diluents by centrifugation, resuspended in fresh supplies of their respective diluent, centrifuged again, and then resuspended in 0.9% NaCl. Ejaculates were also collected into diluent B and stored in the same for 24 hours at 5°C, after which the cells were removed from the diluent by the above-described method. Salisbury et al. disclose that the sperm cells collected in diluent A cease to be motile within approximately two hours, while sperm cells collected in diluent B were immotile on immediate examination after collection and remained so for several hours at room temperature and for at least eight days at 5°C. The cells collected into diluents A and B soon became motile if the carbon dioxide was replaced. Initiation of motility of cells in diluent B could be further stimulated by dilution of the sample with physiological saline solution.

For the reasons stated above, Seidel et al. and Johnson fail to disclose each and every element of the claimed process, as each of these references fails to disclose the staining of sperm cells at a temperature in excess of 40°C. Moreover, neither reference provides any support for, and in fact indicates quite to the contrary, that Applicants have merely optimized a known process. Van Demark et al. or Salisbury et al. do nothing to remedy the failing prima facie obviousness rejection, as Van Demark merely discloses a CO_2 saturated diluent containing sodium citrate dihydrate, sodium bicarbonate, potassium chloride, glucose, sulfanilamide, penicillin dihydrostreptomycin sulfate, and egg yolk for use in sperm storage, and Salisbury et al. merely disclose diluents consisting of $NaHCO_3$, $KHCO_3$, and $C_6H_8O_7 \cdot H_2O$ in water with the gas phase of the same being CO_2, also for sperm storage. Neither reference discloses the staining of viable sperm cells at a temperature in excess of 40°C.

Further demonstrating the nonobviousness of Applicants' claimed method is the fact that Van Demark et al. and Salisbury et al. utilize the disclosed buffers as storage buffers, and in particular, for storage periods of ***one or more days***. Applicants' claimed process is for the staining of sperm cells -- a process that occurs in a matter of minutes

to several hours. Nothing in the cited art would indicate to one skilled in the art the need to use a "storage buffer," and in particular one that is disclosed to be useful for storing sperm cells for a number of days, in a process that takes at most several hours.

Further confirming the nonobviousness of Applicants' claimed invention is the fact that while Van Demark et al. and Salisbury et al. were published some forty plus years prior to the filing of the present application, no one skilled in the art of sperm staining and sorting had combined the storage buffers disclosed in these references with a process for staining sperm. Of particular relevance is that fact that neither Johnson, the inventor of which is credited as pioneering and championing the use of flow cytometry to separate sperm cells into populations of X and Y chromosome bearing cells[49] (a process which first requires the staining of the cells), nor Seidel et al., the two primary references used to support the Office's obviousness rejections, reference such a concept. That is particularly telling, in light of the fact that these references were filed or had a priority date that is approximately ***30 years*** (Johnson) and ***40 years*** (Seidel et al) after the publication of Van Demark et al. and Salisbury et al. In the absence of being able to demonstrate the obviousness of Applicants' claimed invention based on the cited art, the Office has instead utilized Applicants' specification as a template for achieving the claimed invention. This form of "hindsight," however, is neither permissible nor the standard for determining obviousness.[50]

As such, a *prima facie* case of obviousness has not been demonstrated.

Claims 2-15 and 24-28, which depend from claim 1, are patentable over Seidel et al. or Johnson in view of Van Demark et al or Salisbury et al. for the reasons stated with respect to claim 1 and by reason of the additional requirements each claim introduces.

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[49] *See*, for example, D'Occhio (citation, *supra*), at page 250 ("This approach [of sorting sperm cells based on DNA content using flow cytometry] was pioneered and championed by Dr. Larry Johnson of the USDA Germplasm and Gamete Physiology Laboratory, Beltsville, U.S.A. (see Johnson and Pinkel 1986; Johnson 1987; Johnson et al 1999).").

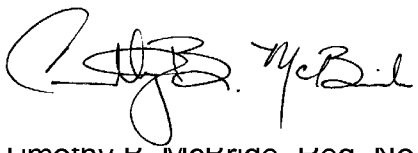
[50] *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1532 (Fed. Cir. 1988); *In re Yates*, 663 F.2d 1054, 1057, 211 U.S.P.Q. 1149, 1151 (C.C.P.A. 1981).

CONCLUSION

In view of the foregoing, Applicants respectfully request withdrawal of the objection of claims 18 and 19 and the rejection claims 1-38 under 35 U.S.C. 103(a), and allowance of all claims as presented herein.

Applicants do not believe that a fee is due for this response, as it is being filed within the three-month shortened statutory period. However, should Applicants be incorrect, the Commissioner is hereby authorized to charge any necessary fee to Deposit Account No. 19-1345.

Respectfully submitted,



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